

Applicant : David H. Coy et al.  
Serial No. :  
Filed :  
Page : 3 of 43

Attorney's Docket No.: 00537-00900L

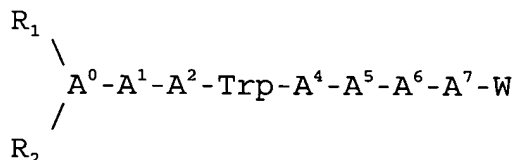
Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-8 (canceled)

9 (new): A method of inhibiting tumor growth which comprises administering to a patient in need thereof an effective amount of a therapeutic peptide of the formula:

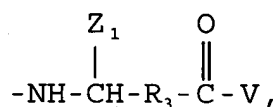


wherein

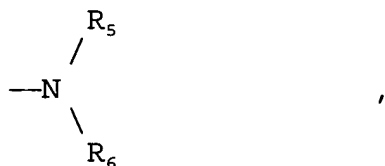
- $A^0$  = Gly, Nle,  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^1$  = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^2$  = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;
- $A^4$  = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;
- $A^5$  = Gln, Asn, Gly, Ala, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>), Trp, Thr, or  $\beta$ -Nal;
- $A^6$  = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;
- $A^7$  = 1-methyl-His, 3-methyl-His or His;

provided that, if  $A^0$  is present,  $A^1$  cannot be pGlu; further provided that, if  $A^0$  or  $A^1$  is present,  $A^2$  cannot be pGlu; further provided that, when  $A^0$  is deleted and  $A^1$  is pGlu,  $R_1$  must be H and  $R_2$  must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

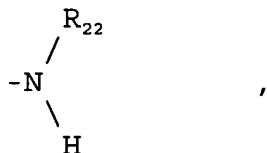
(I):



wherein  $R_3$  is  $CHR_{20}-(CH_2)_{n1}$  (where  $R_{20}$  is either of H or OH; and  $n1$  is either of 1 or 0), or is deleted, and  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH, or  $CH_3$ ),  $F_5$ -Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or  $\beta$ -Nal; and V is either  $OR_4$ , or

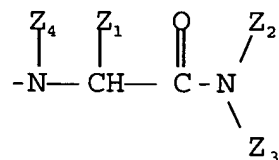


where  $R_4$  is any of  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl, and each  $R_5$ , and  $R_6$ , independently, is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, lower acyl, or



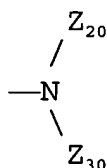
where  $R_{22}$  is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, or lower acyl; provided that, when one of  $R_5$  or  $R_6$  is  $-NR_{22}$ , the other is H;

(II) :



wherein  $\text{Z}_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ),  $\text{F}_5$ -Phe, Trp, Cys, Met, Pro, or HyPro; and each  $\text{Z}_2$ ,  $\text{Z}_3$ , and  $\text{Z}_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III) :



wherein each  $\text{Z}_{20}$  and  $\text{Z}_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $\text{Z}_{20}$  or  $\text{Z}_{30}$  is other than H,  $\text{A}^7$  is His,  $\text{A}^6$  is Gly,  $\text{A}^5$  is Val,  $\text{A}^4$  is Ala,  $\text{A}^2$  is His, and either of  $\text{R}_1$  or  $\text{R}_2$  is other than H,  $\text{A}^1$  must be other than deleted; further provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $\text{R}_1$  and  $\text{R}_2$ , independently, is H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl,  $\text{COE}_1$  (where  $\text{E}_1$  is  $\text{C}_{1-20}$  alkyl,  $\text{C}_{3-20}$  alkenyl,  $\text{C}_{3-20}$  alkynyl, phenyl, naphthyl, or  $\text{C}_{7-10}$

phenylalkyl), or lower acyl, and  $\text{R}_1$  and  $\text{R}_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that

when one of  $R_1$  or  $R_2$  is  $\text{COE}_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.

10 (new): The method of claim 9 wherein said therapeutic peptide is of the formula:

$A^0$  = Gly, D-Phe, or is deleted;

$A^1$  = p-Glu, D-Phe, D-Ala, D- $\beta$ -Nal, D-Cpa, or D-Asn;

$A^2$  = Gln, His, 1-methyl-His, or 3-methyl-His;

$A^4$  = Ala;

$A^5$  = Val;

$A^6$  = Sar, Gly, D-Phe, or D-Ala;

$A^7$  = His;

and, where W is (I) and  $R_3$  is  $\text{CH}_2$  or  $\text{CH}_2\text{-CH}_2$ ,  $Z_1$  is the identifying group of Leu or Phe, where W is (I) and  $R_3$  is  $\text{CHOH-CH}_2$ ,  $Z_1$  is the identifying group of Leu, cyclohexyl-Ala, or Phe and each  $R_5$  and  $R_6$  is H; and where W is (I), V is  $\text{NHR}_6$ , and  $R_6$  is  $\text{NH}_2$ ; where W is (II),  $Z_1$  is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ); and each  $Z_2$ ,  $Z_3$  and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each  $Z_{20}$  and  $Z_{30}$ , is H; and each  $R_1$  and  $R_2$ , independently, is H, lower alkyl, or lower acyl.

11 (new): The method of claim 10 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

12 (new): The method of claim 10 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

13 (new): The method of claim 10 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu-NH<sub>2</sub>.

14 (new): The method of claim 9 wherein said therapeutic peptide is of the formula: W is (I), V is OR<sub>4</sub>, and R<sub>4</sub> is any of C<sub>1-20</sub>alkyl, C<sub>3-20</sub>alkenyl, C<sub>3-20</sub>alkinyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and A<sup>6</sup> is N-methyl-D-Ala or A<sup>1</sup> is D-F<sub>5</sub>-Phe.

15 (new): The therapeutic peptide of claim 14 of the formula:

D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

16 (new): The therapeutic peptide of claim 10 of the formula:

D-Cpa-Gln-Trp-Ala-Val-D-Ala-His- $\beta$ -Leu-NH<sub>2</sub>.

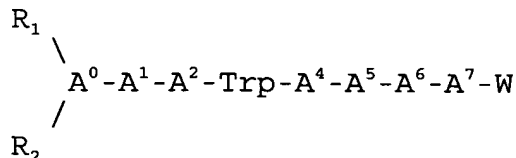
17 (new): The method of claim 9 wherein said tumor is located in the gastrointestinal tract, pancreas, colon, prostate or breast.

18 (new): The method of claim 9 wherein said tumor is a small-cell lung carcinoma.

19 (new): The method of claim 9 wherein said effective amount is 0.5  $\mu$ g/kg/day to 5 mg/kg/day.

20 (new): The method of claim 9 wherein said effective amount is 250 mg/patient/day.

21 (new): A method of inhibiting pancreatic adenocarcinomas which comprises administering to a patient in need thereof an effective amount of a therapeutic compound of the formula:

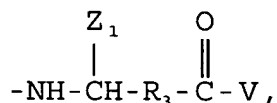


wherein

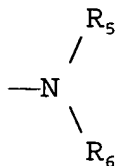
- $A^0$  = Gly, Nle,  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^1$  = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^2$  = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;
- $A^4$  = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;
- $A^5$  = Gln, Asn, Gly, Ala, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>), Trp, Thr, or  $\beta$ -Nal;
- $A^6$  = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;
- $A^7$  = 1-methyl-His, 3-methyl-His or His;
- provided that, if  $A^0$  is present,  $A^1$  cannot be pGlu; further provided that, if  $A^0$  or  $A^1$  is present,  $A^2$  cannot be pGlu; further provided

that, when  $A^0$  is deleted and  $A^1$  is pGlu,  $R_1$  must be H and  $R_2$  must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

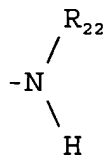
(I):



wherein  $R_3$  is  $CHR_{20}-(CH_2)_{n1}$  (where  $R_{20}$  is either of H or OH; and  $n1$  is either of 1 or 0), or is deleted, and  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH, or  $CH_3$ ),  $F_5$ -Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or  $\beta$ -Nal; and V is either  $OR_4$ , or



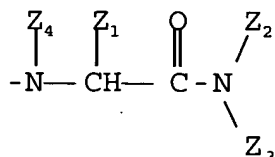
where  $R_4$  is any of  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl, and each  $R_5$ , and  $R_6$ , independently, is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, lower acyl, or



where  $R_{22}$  is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, or lower acyl; provided that, when one of  $R_5$  or  $R_6$  is  $-NR_{22}$ , the other is H;

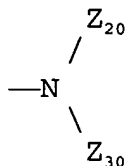


(II) :



wherein  $\text{Z}_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ),  $\text{F}_5$ -Phe, Trp, Cys, Met, Pro, or HyPro; and each  $\text{Z}_2$ ,  $\text{Z}_3$ , and  $\text{Z}_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III) :



wherein each  $\text{Z}_{20}$  and  $\text{Z}_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $\text{Z}_{20}$  or  $\text{Z}_{30}$  is other than H,  $\text{A}^7$  is His,  $\text{A}^6$  is Gly,  $\text{A}^5$  is Val,  $\text{A}^4$  is Ala,  $\text{A}^2$  is His, and either of  $\text{R}_1$  or  $\text{R}_2$  is other than H,  $\text{A}^1$  must be other than deleted; further provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $\text{R}_1$  and  $\text{R}_2$ , independently, is H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl,  $\text{COE}_1$  (where  $\text{E}_1$  is  $\text{C}_{1-20}$  alkyl,  $\text{C}_{3-20}$  alkenyl,  $\text{C}_{3-20}$  alkynyl, phenyl, naphthyl, or  $\text{C}_{7-10}$  phenylalkyl), or lower acyl, and  $\text{R}_1$  and  $\text{R}_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that when one of  $\text{R}_1$  or  $\text{R}_2$  is  $\text{COE}_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.

22 (new): The method of claim 21 wherein said therapeutic peptide is of the formula:

$A^0$  = Gly, D-Phe, or is deleted;

$A^1$  = p-Glu, D-Phe, D-Ala, D- $\beta$ -Nal, D-Cpa, or D-Asn;

$A^2$  = Gln, His, 1-methyl-His, or 3-methyl-His;

$A^4$  = Ala;

$A^5$  = Val;

$A^6$  = Sar, Gly, D-Phe, or D-Ala;

$A^7$  = His;

and, where W is (I) and  $R_3$  is  $CH_2$  or  $CH_2-CH_2$ ,  $Z_1$  is the identifying group of Leu or Phe, where W is (I) and  $R_3$  is  $CHOH-CH_2$ ,  $Z_1$  is the identifying group of Leu, cyclohexyl-Ala, or Phe and each  $R_5$  and  $R_6$  is H; and where W is (I), V is  $NHR_6$ , and  $R_6$  is  $NH_2$ ; where W is (II),  $Z_1$  is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH or  $CH_3$ ); and each  $Z_2$ ,  $Z_3$  and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each  $Z_{20}$  and  $Z_{30}$ , is H; and each  $R_1$  and  $R_2$ , independently, is H, lower alkyl, or lower acyl.

23 (new): The method of claim 22 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

24 (new): The method of claim 22 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

25 (new): The method of claim 22 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu- $NH_2$ .

26 (new): The method of claim 21 wherein said therapeutic peptide is of the formula: W is (I), V is OR<sub>4</sub>, and R<sub>4</sub> is any of C<sub>1-20</sub>alkyl, C<sub>3-20</sub>alkenyl, C<sub>3-20</sub>alkinyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and A<sup>6</sup> is N-methyl-D-Ala or A<sup>1</sup> is D-F<sub>5</sub>-Phe.

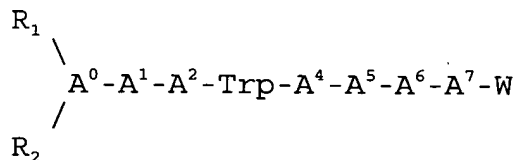
27 (new): The therapeutic peptide of claim 26 of the formula:  
D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

28 (new): The therapeutic peptide of claim 22 of the formula:  
D-Cpa-Gln-Trp-Ala-Val-D-Ala-His-β-Leu-NH<sub>2</sub>.

29 (new): The method of claim 21 wherein said effective amount is 0.5 μg/kg/day to 5 mg/kg/day.

30 (new): The method of claim 21 wherein said effective amount is 250 mg/patient/day.

31 (new): A method of inhibiting gastric acid secretion which comprises administering to a patient in need thereof an effective amount of a therapeutic compound of the formula:



wherein

A<sup>0</sup> = Gly, Nle, α-aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or β-Nal, or is deleted;

A<sup>1</sup> = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;

A<sup>2</sup> = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;

A<sup>4</sup> = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;

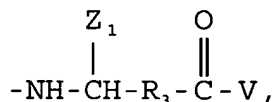
A<sup>5</sup> = Gln, Asn, Gly, Ala, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>), Trp, Thr, or  $\beta$ -Nal;

A<sup>6</sup> = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;

A<sup>7</sup> = 1-methyl-His, 3-methyl-His or His;

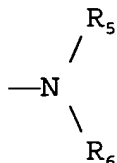
provided that, if A<sup>0</sup> is present, A<sup>1</sup> cannot be pGlu; further provided that, if A<sup>0</sup> or A<sup>1</sup> is present, A<sup>2</sup> cannot be pGlu; further provided that, when A<sup>0</sup> is deleted and A<sup>1</sup> is pGlu, R<sub>1</sub> must be H and R<sub>2</sub> must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

(I):

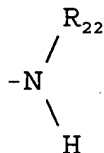


wherein R<sub>3</sub> is CHR<sub>20</sub>-(CH<sub>2</sub>)<sub>n1</sub> (where R<sub>20</sub> is either of H or OH; and n1 is either of 1 or 0), or is deleted, and Z<sub>1</sub> is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser,

Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH, or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or β-Nal; and V is either OR<sub>4</sub>, or

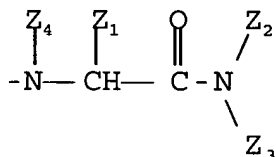


where R<sub>4</sub> is any of C<sub>1-20</sub> alkyl, C<sub>3-20</sub> alkenyl, C<sub>3-20</sub> alkynyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and each R<sub>5</sub>, and R<sub>6</sub>, independently, is any of H, C<sub>1-12</sub> alkyl, C<sub>7-10</sub> phenylalkyl, lower acyl, or



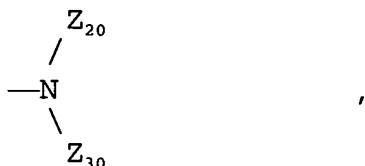
where R<sub>22</sub> is any of H, C<sub>1-12</sub> alkyl, C<sub>7-10</sub> phenylalkyl, or lower acyl; provided that, when one of R<sub>5</sub> or R<sub>6</sub> is -NR<sub>22</sub>, the other is H;

(II):



wherein Z<sub>1</sub> is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu, β-Nal, Gln, p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, Met, Pro, or HyPro; and each Z<sub>2</sub>, Z<sub>3</sub>, and Z<sub>4</sub>, independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III) :



wherein each  $\text{Z}_{20}$  and  $\text{Z}_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $\text{Z}_{20}$  or  $\text{Z}_{30}$  is other than H,  $\text{A}^7$  is His,  $\text{A}^6$  is Gly,  $\text{A}^5$  is Val,  $\text{A}^4$  is Ala,  $\text{A}^2$  is His, and either of  $\text{R}_1$  or  $\text{R}_2$  is other than H,  $\text{A}^1$  must be other than deleted; further provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $\text{R}_1$  and  $\text{R}_2$ , independently, is H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl,  $\text{COE}_1$  (where  $\text{E}_1$  is  $\text{C}_{1-20}$  alkyl,  $\text{C}_{3-20}$  alkenyl,  $\text{C}_{3-20}$  alkynyl, phenyl, naphthyl, or  $\text{C}_{7-10}$  phenylalkyl), or lower acyl, and  $\text{R}_1$  and  $\text{R}_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that when one of  $\text{R}_1$  or  $\text{R}_2$  is  $\text{COE}_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.

32 (new): The method of claim 31 wherein said therapeutic peptide is of the formula:

$\text{A}^0$  = Gly, D-Phe, or is deleted;

$\text{A}^1$  = p-Glu, D-Phe, D-Ala, D- $\beta$ -Nal, D-Cpa, or D-Asn;

$\text{A}^2$  = Gln, His, 1-methyl-His, or 3-methyl-His;

$\text{A}^4$  = Ala;

$\text{A}^5$  = Val;

$\text{A}^6$  = Sar, Gly, D-Phe, or D-Ala;

$\text{A}^7$  = His;

and, where W is (I) and  $R_3$  is  $\text{CH}_2$  or  $\text{CH}_2\text{-CH}_2$ ,  $Z_1$  is the identifying group of Leu or Phe, where W is (I) and  $R_3$  is  $\text{CHOH-CH}_2$ ,  $Z_1$  is the identifying group of Leu, cyclohexyl-Ala,

or Phe and each  $R_5$  and  $R_6$  is H; and where W is (I), V is  $\text{NHR}_6$ , and  $R_6$  is  $\text{NH}_2$ ; where W is (II),  $Z_1$  is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ); and each  $Z_2$ ,  $Z_3$  and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each  $Z_{20}$  and  $Z_{30}$ , is H; and each  $R_1$  and  $R_2$ , independently, is H, lower alkyl, or lower acyl.

33 (new): The method of claim 32 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

34 (new): The method of claim 32 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

35 (new): The method of claim 32 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu- $\text{NH}_2$ .

36 (new): The method of claim 31 wherein said therapeutic peptide is of the formula: W is (I), V is  $\text{OR}_4$ , and  $R_4$  is any of  $\text{C}_{1-20}$ alkyl,  $\text{C}_{3-20}$ alkenyl,  $\text{C}_{3-20}$ alkinyl, phenyl, naphthyl, or  $\text{C}_{7-10}$ phenylalkyl, and  $\text{A}^6$  is N-methyl-D-Ala or  $\text{A}^1$  is D- $\text{F}_5$ -Phe.

37 (new): The therapeutic peptide of claim 36 of the formula:

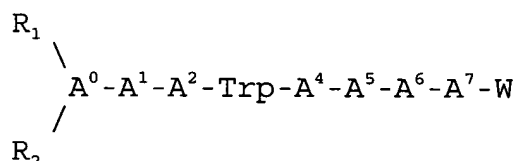
D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

38 (new): The therapeutic peptide of claim 32 of the formula:

D-Cpa-Gln-Trp-Ala-Val-D-Ala-His- $\beta$ -Leu-NH<sub>2</sub>.

39 (new): The method of claim 31 wherein said effective amount is 0.5  $\mu$ g/kg/day to 5 mg/kg/day.

40 (new): A method of treating motility disorders of the GI tract which comprises administering to a patient in need thereof an effective amount of a therapeutic compound of the formula:



wherein

A<sup>0</sup> = Gly, Nle,  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal, or is deleted;

A<sup>1</sup> = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;

A<sup>2</sup> = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;

A<sup>4</sup> = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;

A<sup>5</sup> = Gln, Asn, Gly, Ala, Leu, Ile, Nle,  $\alpha$ -aminobutyric



acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>), Trp, Thr, or β-Nal;

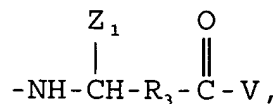
A<sup>6</sup> = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or β-Nal;

A<sup>7</sup> = 1-methyl-His, 3-methyl-His or His;

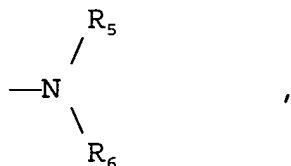
provided that, if A<sup>0</sup> is present, A<sup>1</sup> cannot be pGlu; further provided that, if A<sup>0</sup> or A<sup>1</sup> is present, A<sup>2</sup> cannot be pGlu;

further provided that, when A<sup>0</sup> is deleted and A<sup>1</sup> is pGlu, R<sub>1</sub> must be H and R<sub>2</sub> must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

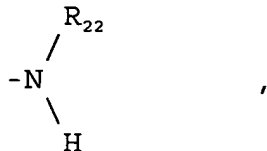
(I):



wherein R<sub>3</sub> is CHR<sub>20</sub>-(CH<sub>2</sub>)<sub>n1</sub> (where R<sub>20</sub> is either of H or OH; and n1 is either of 1 or 0), or is deleted, and Z<sub>1</sub> is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH, or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or β-Nal; and V is either OR<sub>4</sub>, or

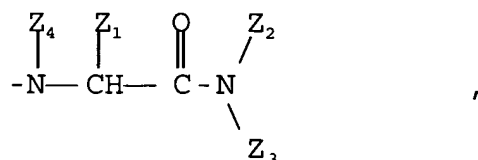


where R<sub>4</sub> is any of C<sub>1-20</sub> alkyl, C<sub>3-20</sub> alkenyl, C<sub>3-20</sub> alkynyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and each R<sub>5</sub>, and R<sub>6</sub>, independently, is any of H, C<sub>1-12</sub> alkyl, C<sub>7-10</sub> phenylalkyl, lower acyl, or



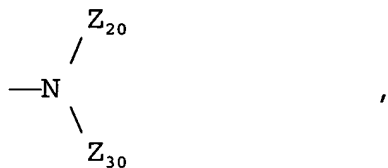
where  $\text{R}_{22}$  is any of H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl, or lower acyl; provided that, when one of  $\text{R}_5$  or  $\text{R}_6$  is  $-\text{NR}_{22}$ , the other is H;

(II):



wherein  $\text{Z}_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ),  $\text{F}_5$ -Phe, Trp, Cys, Met, Pro, or HyPro; and each  $\text{Z}_2$ ,  $\text{Z}_3$ , and  $\text{Z}_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III):



wherein each  $\text{Z}_{20}$  and  $\text{Z}_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $\text{Z}_{20}$  or  $\text{Z}_{30}$  is other than H,  $\text{A}^7$  is His,  $\text{A}^6$  is Gly,  $\text{A}^5$  is Val,  $\text{A}^4$  is Ala,  $\text{A}^2$  is His, and either of  $\text{R}_1$  or  $\text{R}_2$  is other than H,  $\text{A}^1$  must be other than deleted; further provided that, for the

formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $R_1$  and  $R_2$ , independently, is H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl,  $COE_1$  (where  $E_1$  is  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl), or lower acyl, and  $R_1$  and  $R_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that when one of  $R_1$  or  $R_2$  is  $COE_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.

41 (new): The method of claim 40 wherein said therapeutic peptide is of the formula:

$A^0$  = Gly, D-Phe, or is deleted;

$A^1$  = p-Glu, D-Phe, D-Ala, D- $\beta$ -Nal, D-Cpa, or D-Asn;

$A^2$  = Gln, His, 1-methyl-His, or 3-methyl-His;

$A^4$  = Ala;

$A^5$  = Val;

$A^6$  = Sar, Gly, D-Phe, or D-Ala;

$A^7$  = His;

and, where W is (I) and  $R_3$  is  $CH_2$  or  $CH_2-CH_2$ ,  $Z_1$  is the identifying group of Leu or Phe, where W is (I) and  $R_3$  is  $CHOH-CH_2$ ,  $Z_1$  is the identifying group of Leu, cyclohexyl-Ala, or Phe and each  $R_5$  and  $R_6$  is H; and where W is (I), V is  $NHR_6$ , and  $R_6$  is  $NH_2$ ; where W is (II),  $Z_1$  is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH or  $CH_3$ ); and each  $Z_2$ ,  $Z_3$  and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each  $Z_{20}$  and  $Z_{30}$ , is H; and each  $R_1$  and  $R_2$ , independently, is H, lower alkyl, or lower acyl.

42 (new): The method of claim 41 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

43 (new): The method of claim 41 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

44 (new): The method of claim 41 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu-NH<sub>2</sub>.

45 (new): The method of claim 40 wherein said therapeutic peptide is of the formula: W is (I), V is OR<sub>4</sub>, and R<sub>4</sub> is any of C<sub>1-20</sub>alkyl, C<sub>3-20</sub>alkenyl, C<sub>3-20</sub>alkinyl, phenyl,

naphthyl, or C<sub>7-10</sub> phenylalkyl, and A<sup>6</sup> is N-methyl-D-Ala or A<sup>1</sup> is D-F<sub>5</sub>-Phe.

46 (new): The therapeutic peptide of claim 45 of the formula:

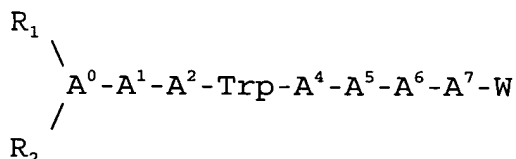
D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

47 (new): The therapeutic peptide of claim 41 of the formula:

D-Cpa-Gln-Trp-Ala-Val-D-Ala-His- $\beta$ -Leu-NH<sub>2</sub>.

48. (new): The method of claim 40 wherein said effective amount is 0.5  $\mu$ g/kg/day to 5 mg/kg/day.

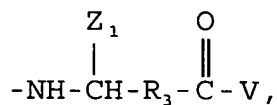
49 (new): A method of suppressing amylase release which comprises administering to a patient in need thereof an effective amount of a therapeutic peptide of the formula:



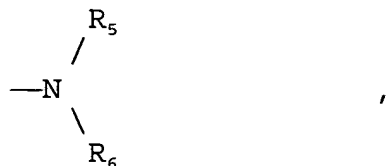
wherein

- $A^0$  = Gly, Nle,  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^1$  = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^2$  = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;
- $A^4$  = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;
- $A^5$  = Gln, Asn, Gly, Ala, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>), Trp, Thr, or  $\beta$ -Nal;
- $A^6$  = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal;
- $A^7$  = 1-methyl-His, 3-methyl-His or His;
- provided that, if  $A^0$  is present,  $A^1$  cannot be pGlu; further provided that, if  $A^0$  or  $A^1$  is present,  $A^2$  cannot be pGlu; further provided that, when  $A^0$  is deleted and  $A^1$  is pGlu, R<sub>1</sub> must be H and R<sub>2</sub> must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

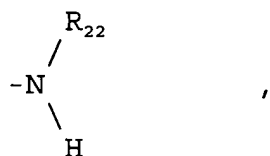
(I) :



wherein R<sub>3</sub> is CHR<sub>20</sub>-(CH<sub>2</sub>)<sub>n1</sub> (where R<sub>20</sub> is either of H or OH; and n1 is either of 1 or 0), or is deleted, and Z<sub>1</sub> is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH, or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or β-Nal; and V is either OR<sub>4</sub>, or

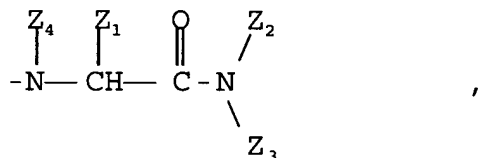


where R<sub>4</sub> is any of C<sub>1-20</sub> alkyl, C<sub>3-20</sub> alkenyl, C<sub>3-20</sub> alkynyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and each R<sub>5</sub>, and R<sub>6</sub>, independently, is any of H, C<sub>1-12</sub> alkyl, C<sub>7-10</sub> phenylalkyl, lower acyl, or



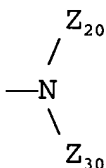
where R<sub>22</sub> is any of H, C<sub>1-12</sub> alkyl, C<sub>7-10</sub> phenylalkyl, or lower acyl; provided that, when one of R<sub>5</sub> or R<sub>6</sub> is -NR<sub>22</sub>, the other is H;

(II) :



wherein  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ),  $\text{F}_5$ -Phe, Trp, Cys, Met, Pro, or HyPro; and each  $Z_2$ ,  $Z_3$ , and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III):



wherein each  $Z_{20}$  and  $Z_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $Z_{20}$  or  $Z_{30}$  is other than H,  $A^7$  is His,  $A^6$  is Gly,  $A^5$  is Val,  $A^4$  is Ala,  $A^2$  is His, and either of  $R_1$  or  $R_2$  is other than H,  $A^1$  must be other than deleted; further provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $R_1$  and  $R_2$ , independently, is H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl,  $\text{COE}_1$  (where  $E_1$  is  $\text{C}_{1-20}$  alkyl,  $\text{C}_{3-20}$  alkenyl,  $\text{C}_{3-20}$  alkynyl, phenyl, naphthyl, or  $\text{C}_{7-10}$  phenylalkyl), or lower acyl, and  $R_1$  and  $R_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that when one of  $R_1$  or  $R_2$  is  $\text{COE}_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.

50 (new): The method of claim 49 wherein said therapeutic peptide is of the formula:

$A^0$  = Gly, D-Phe, or is deleted;

$A^1$  = p-Glu, D-Phe, D-Ala, D- $\beta$ -Nal, D-Cpa, or D-Asn;

$A^2$  = Gln, His, 1-methyl-His, or 3-methyl-His;

$A^4$  = Ala;

$A^5$  = Val;

$A^6$  = Sar, Gly, D-Phe, or D-Ala;

$A^7$  = His;

and, where W is (I) and  $R_3$  is  $CH_2$  or  $CH_2-CH_2$ ,  $Z_1$  is the identifying group of Leu or Phe, where W is (I) and  $R_3$  is  $CHOH-CH_2$ ,  $Z_1$  is the identifying group of Leu, cyclohexyl-Ala,

or Phe and each  $R_5$  and  $R_6$  is H; and where W is (I), V is  $NHR_6$ , and  $R_6$  is  $NH_2$ ; where W is (II),  $Z_1$  is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH or  $CH_3$ ); and each  $Z_2$ ,  $Z_3$  and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each  $Z_{20}$  and  $Z_{30}$ , is H; and each  $R_1$  and  $R_2$ , independently, is H, lower alkyl, or lower acyl.

51 (new): The method of claim 50 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

52 (new): The method of claim 50 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

53 (new): The method of claim 50 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu- $NH_2$ .

54 (new): The method of claim 49 wherein said therapeutic peptide is of the formula: W is (I), V is  $OR_4$ , and  $R_4$  is any of  $C_{1-20}$ alkyl,  $C_{3-20}$ alkenyl,  $C_{3-20}$ alkinyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl, and  $A^6$  is N-methyl-D-Ala or  $A^1$  is D-F<sub>5</sub>-Phe.



55 (new): The therapeutic peptide of claim 54 of the formula:

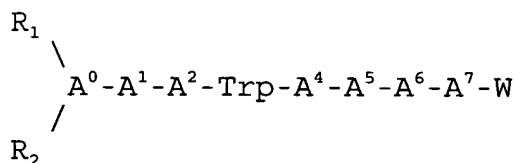
D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

56 (new): The therapeutic peptide of claim 50 of the formula:

D-Cpa-Gln-Trp-Ala-Val-D-Ala-His- $\beta$ -Leu-NH<sub>2</sub>.

57 (new): The method of claim 49 wherein said effective amount is 0.5  $\mu$ g/kg/day to 5 mg/kg/day.

58 (new): A method of treating cancer cachexia which comprises administering to a patient in need thereof an effective amount of a therapeutic compound of the formula:



wherein

A<sup>0</sup> = Gly, Nle,  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or  $\beta$ -Nal, or is deleted;

A<sup>1</sup> = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;

A<sup>2</sup> = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;

A<sup>4</sup> = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric

acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>),  
Trp, Cys, or β-Nal;

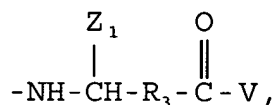
A<sup>5</sup> = Gln, Asn, Gly, Ala, Leu, Ile, Nle, α-aminobutyric  
acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>),  
Trp, Thr, or β-Nal;

A<sup>6</sup> = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val,  
Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>,  
OH, H or CH<sub>3</sub>), Trp, Cys, or β-Nal;

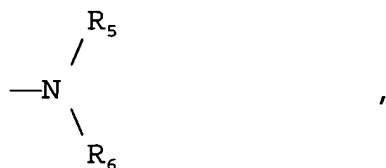
A<sup>7</sup> = 1-methyl-His, 3-methyl-His or His;

provided that, if A<sup>0</sup> is present, A<sup>1</sup> cannot be pGlu; further provided  
that, if A<sup>0</sup> or A<sup>1</sup> is present, A<sup>2</sup> cannot be pGlu; further provided  
that, when A<sup>0</sup> is deleted and A<sup>1</sup> is pGlu, R<sub>1</sub> must be H and R<sub>2</sub> must be  
the portion of Glu that forms the imine ring in pGlu; and further  
provided that, W can be any one of the following:

(I):

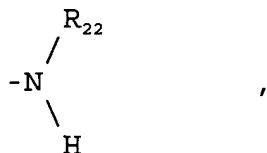


wherein R<sub>3</sub> is CHR<sub>20</sub>-(CH<sub>2</sub>)<sub>n1</sub> (where R<sub>20</sub> is either of H or OH; and n1  
is either of 1 or 0), or is deleted, and Z<sub>1</sub> is the identifying  
group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser,  
Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH, or  
CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or β-  
Nal; and V is either OR<sub>4</sub>, or



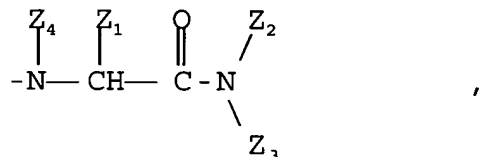
where  $R_4$  is any of  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl, and each  $R_5$ , and  $R_6$ , independently, is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, lower acyl, or

Applicant : Coy et al.



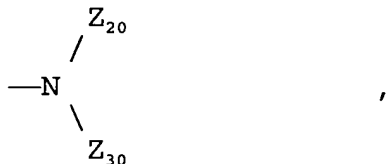
where  $R_{22}$  is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, or lower acyl; provided that, when one of  $R_5$  or  $R_6$  is  $-NR_{22}$ , the other is H;

(II):



wherein  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH or  $CH_3$ ),  $F_5$ -Phe, Trp, Cys, Met, Pro, or HyPro; and each  $Z_2$ ,  $Z_3$ , and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III):



wherein each  $Z_{20}$  and  $Z_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when

either of  $Z_{20}$  or  $Z_{30}$  is other than H,  $A^7$  is His,  $A^6$  is Gly,  $A^5$  is Val,  $A^4$  is Ala,  $A^2$  is His, and either of  $R_1$  or  $R_2$  is other than H,  $A^1$  must be other than deleted; further

provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $R_1$  and  $R_2$ , independently, is H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl,  $COE_1$  (where  $E_1$  is  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl), or lower acyl, and  $R_1$  and  $R_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that when one of  $R_1$  or  $R_2$  is  $COE_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.

59 (new): The method of claim 58 wherein said therapeutic peptide is of the formula:

$A^0$  = Gly, D-Phe, or is deleted;

$A^1$  = p-Glu, D-Phe, D-Ala, D- $\beta$ -Nal, D-Cpa, or D-Asn;

$A^2$  = Gln, His, 1-methyl-His, or 3-methyl-His;

$A^4$  = Ala;

$A^5$  = Val;

$A^6$  = Sar, Gly, D-Phe, or D-Ala;

$A^7$  = His;

and, where W is (I) and  $R_3$  is  $CH_2$  or  $CH_2-CH_2$ ,  $Z_1$  is the identifying group of Leu or Phe, where W is (I) and  $R_3$  is  $CHOH-CH_2$ ,  $Z_1$  is the identifying group of Leu, cyclohexyl-Ala, or Phe and each  $R_5$  and  $R_6$  is H; and where W is (I), V is  $NHR_6$ , and  $R_6$  is  $NH_2$ ; where W is (II),  $Z_1$  is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH or  $CH_3$ ); and each  $Z_2$ ,  $Z_3$  and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each  $Z_{20}$  and  $Z_{30}$ , is H; and each  $R_1$  and  $R_2$ , independently, is H, lower alkyl, or lower acyl.

60 (new): The method of claim 59 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

61 (new): The method of claim 59 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

62 (new): The method of claim 59 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu-NH<sub>2</sub>.

63 (new): The method of claim 58 wherein said therapeutic peptide is of the formula: W is (I), V is OR<sub>4</sub>, and R<sub>4</sub> is any of C<sub>1-20</sub>alkyl, C<sub>3-20</sub>alkenyl, C<sub>3-20</sub>alkinyl, phenyl, naphthyl, or C<sub>7-10</sub>phenylalkyl, and A<sup>6</sup> is N-methyl-D-Ala or A<sup>1</sup> is D-F<sub>5</sub>-Phe.

64 (new): The therapeutic peptide of claim 63 of the formula:

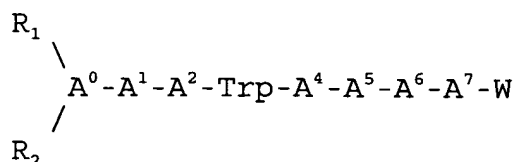
D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

65 (new): The therapeutic peptide of claim 59 of the formula:

D-Cpa-Gln-Trp-Ala-Val-D-Ala-His- $\beta$ -Leu-NH<sub>2</sub>.

66 (new): The method of claim 58 wherein said effective amount is 0.5  $\mu$ g/kg/day to 5 mg/kg/day.

67 (new): A method of inhibiting growth hormone release which comprises administering to a patient in need thereof an effective amount of a therapeutic peptide of the formula:

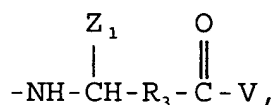


wherein

- $A^0$  = Gly, Nle,  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br,  $NO_2$ , OH, H or  $CH_3$ ), Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^1$  = the D or L-isomer of any of pGlu, Nle, or  $\alpha$ -aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br,  $NO_2$ , OH, H or  $CH_3$ ),  $F_5$ -Phe, Trp, Cys, or  $\beta$ -Nal, or is deleted;
- $A^2$  = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br,  $NO_2$ , OH, H or  $CH_3$ ), Trp, Cys,  $\beta$ -Nal, His, 1-methyl-His, or 3-methyl-His;
- $A^4$  = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br,  $NO_2$ , OH, H or  $CH_3$ ), Trp, Cys, or  $\beta$ -Nal;
- $A^5$  = Gln, Asn, Gly, Ala, Leu, Ile, Nle,  $\alpha$ -aminobutyric acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or  $CH_3$ ), Trp, Thr, or  $\beta$ -Nal;
- $A^6$  = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br,  $NO_2$ , OH, H or  $CH_3$ ), Trp, Cys, or  $\beta$ -Nal;
- $A^7$  = 1-methyl-His, 3-methyl-His or His;

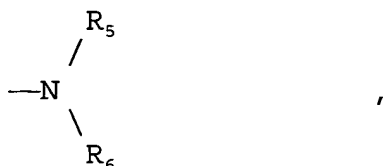
provided that, if  $A^0$  is present,  $A^1$  cannot be pGlu; further provided that, if  $A^0$  or  $A^1$  is present,  $A^2$  cannot be pGlu; further provided that, when  $A^0$  is deleted and  $A^1$  is pGlu,  $R_1$  must be H and  $R_2$  must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

(I):

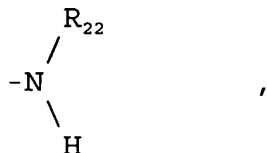


wherein  $R_3$  is  $CHR_{20}-(CH_2)_{n1}$  (where  $R_{20}$  is either of H or OH; and  $n1$  is either of 1 or 0), or is deleted, and  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val,

Leu, Ile, Ser, Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH, or  $CH_3$ ),  $F_5$ -Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or  $\beta$ -Nal; and V is either  $OR_4$ , or

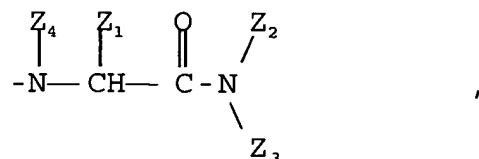


where  $R_4$  is any of  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or  $C_{7-10}$  phenylalkyl, and each  $R_5$ , and  $R_6$ , independently, is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, lower acyl, or



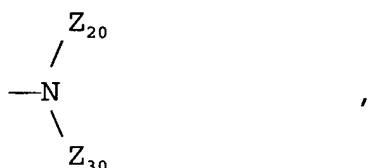
where  $R_{22}$  is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, or lower acyl; provided that, when one of  $R_5$  or  $R_6$  is  $-NR_{22}$ , the other is H;

(II) :



wherein  $\text{Z}_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH or  $\text{CH}_3$ ), F<sub>5</sub>-Phe, Trp, Cys, Met, Pro, or HyPro; and each  $\text{Z}_2$ ,  $\text{Z}_3$ , and  $\text{Z}_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III) :



wherein each  $\text{Z}_{20}$  and  $\text{Z}_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $\text{Z}_{20}$  or  $\text{Z}_{30}$  is other than H,  $\text{A}^7$  is His,  $\text{A}^6$  is Gly,  $\text{A}^5$  is Val,  $\text{A}^4$  is Ala,  $\text{A}^2$  is His, and either of  $\text{R}_1$  or  $\text{R}_2$  is other than H,  $\text{A}^1$  must be other than deleted; further provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $\text{R}_1$  and  $\text{R}_2$ , independently, is H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl,  $\text{COE}_1$  (where  $\text{E}_1$  is  $\text{C}_{1-20}$  alkyl,  $\text{C}_{3-20}$  alkenyl,  $\text{C}_{3-20}$  alkynyl, phenyl, naphthyl, or  $\text{C}_{7-10}$  phenylalkyl), or lower acyl, and  $\text{R}_1$  and  $\text{R}_2$  are bonded to the N-terminal amino acid of said peptide, and further provided that when one of  $\text{R}_1$  or  $\text{R}_2$  is  $\text{COE}_1$ , the other must be H, or a pharmaceutically acceptable salt thereof.



68 (new): The method of claim 67 wherein said therapeutic peptide is of the formula:

A<sup>0</sup> = Gly, D-Phe, or is deleted;

A<sup>1</sup> = p-Glu, D-Phe, D-Ala, D-β-Nal, D-Cpa, or D-Asn;

A<sup>2</sup> = Gln, His, 1-methyl-His, or 3-methyl-His;

A<sup>4</sup> = Ala;

A<sup>5</sup> = Val;

A<sup>6</sup> = Sar, Gly, D-Phe, or D-Ala;

A<sup>7</sup> = His;

and, where W is (I) and R<sub>3</sub> is CH<sub>2</sub> or CH<sub>2</sub>-CH<sub>2</sub>, Z<sub>1</sub> is the identifying group of Leu or Phe, where W is (I) and R<sub>3</sub> is CHOH-CH<sub>2</sub>, Z<sub>1</sub> is the identifying group of Leu, cyclohexyl-Ala,

or Phe and each R<sub>5</sub> and R<sub>6</sub> is H; and where W is (I), V is NHR<sub>6</sub>, and R<sub>6</sub> is NH<sub>2</sub>; where W is (II), Z<sub>1</sub> is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH or CH<sub>3</sub>); and each Z<sub>2</sub>, Z<sub>3</sub> and Z<sub>4</sub>, independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each Z<sub>20</sub> and Z<sub>30</sub>, is H; and each R<sub>1</sub> and R<sub>2</sub>, independently, is H, lower alkyl, or lower acyl.

69 (new): The method of claim 68 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

70 (new): The method of claim 68 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

71 (new): The method of claim 68 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His-β-Leu-NH<sub>2</sub>.

72 (new): The method of claim 67 wherein said therapeutic peptide is of the formula: W is (I), V is OR<sub>4</sub>, and R<sub>4</sub> is any of C<sub>1-20</sub>alkyl, C<sub>3-20</sub>alkenyl, C<sub>3-20</sub>alkinyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and A<sup>6</sup> is N-methyl-D-Ala or A<sup>1</sup> is D-F<sub>5</sub>-Phe.

73 (new): The therapeutic peptide of claim 72 of the formula:  
D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

74 (new): The therapeutic peptide of claim 68 of the formula:  
D-Cpa-Gln-Trp-Ala-Val-D-Ala-His-β-Leu-NH<sub>2</sub>.

75 (new): The method of claim 67 wherein said growth hormone is a factor in the progression of muscular dystrophy in a patient.

76 (new): The method of claim 67 wherein said growth hormone is a factor in the onset of diabetes in a patient.

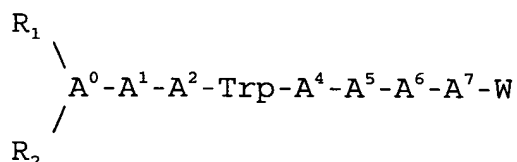
77 (new): The method of claim 67 wherein said growth hormone is a factor in the development of diabetes-related retinopathy in a patient.

78 (new): The method of claim 67 wherein said effective amount is 0.5 µg/kg/day to 5 mg/kg/day.

79 (new): The method of claim 67 wherein said effective amount is 0.01 µg/kg/day to 1000 µg/kg/day.

80 (new): The method of claim 67 wherein said effective amount is 0.1 µg/kg/day to 100 µg/kg/day.

81 (new): A method of treating arteriosclerosis which comprises administering to a patient in need thereof an effective amount of a therapeutic peptide of the formula:



wherein

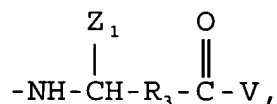
- A<sup>0</sup> = Gly, Nle, α-aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or β-Nal, or is deleted;
- A<sup>1</sup> = the D or L-isomer of any of pGlu, Nle, or α-aminobutyric acid, or the D-isomer of any of Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), F<sub>5</sub>-Phe, Trp, Cys, or β-Nal, or is deleted;
- A<sup>2</sup> = pGlu, Gly, Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, β-Nal, His, 1-methyl-His, or 3-methyl-His;
- A<sup>4</sup> = Ala, Val, Gln, Asn, Gly, Leu, Ile, Nle, α-aminobutyric acid, Met, p-X-Phe (where X = F, Cl, Br, NO<sub>2</sub>, OH, H or CH<sub>3</sub>), Trp, Cys, or β-Nal;
- A<sup>5</sup> = Gln, Asn, Gly, Ala, Leu, Ile, Nle, α-aminobutyric acid, Met, Val, p-X-Phe (where X = F, Cl, Br, OH, H or CH<sub>3</sub>), Trp, Thr, or β-Nal;

$A^6$  = Sar, Gly, or the D-isomer of any of Ala, N-methyl-Ala, Val, Gln, Asn, Leu, Ile, Met, p-X-Phe (where X = F, Cl, Br,  $\text{NO}_2$ , OH, H or  $\text{CH}_3$ ), Trp, Cys, or  $\beta$ -Nal;

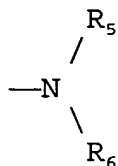
$A^7$  = 1-methyl-His, 3-methyl-His or His;

provided that, if  $A^0$  is present,  $A^1$  cannot be pGlu; further provided that, if  $A^0$  or  $A^1$  is present,  $A^2$  cannot be pGlu; further provided that, when  $A^0$  is deleted and  $A^1$  is pGlu,  $R_1$  must be H and  $R_2$  must be the portion of Glu that forms the imine ring in pGlu; and further provided that, W can be any one of the following:

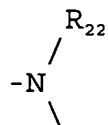
(I):



wherein  $R_3$  is  $\text{CHR}_{20}\text{-(CH}_2\text{)}_{n1}$  (where  $R_{20}$  is either of H or OH; and  $n1$  is either of 1 or 0), or is deleted, and  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu, Gln, p-X-Phe (where X = H, F, Cl, Br,  $\text{NO}_2$ , OH, or  $\text{CH}_3$ ),  $\text{F}_5$ -Phe, Trp, Cys, Met, Pro, HyPro, cyclohexyl-Ala, or  $\beta$ -Nal; and V is either  $\text{OR}_4$ , or



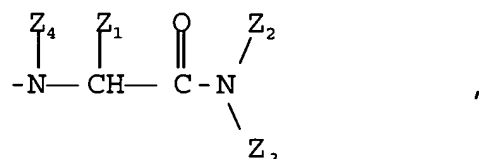
where  $R_4$  is any of  $\text{C}_{1-20}$  alkyl,  $\text{C}_{3-20}$  alkenyl,  $\text{C}_{3-20}$  alkynyl, phenyl, naphthyl, or  $\text{C}_{7-10}$  phenylalkyl, and each  $R_5$ , and  $R_6$ , independently, is any of H,  $\text{C}_{1-12}$  alkyl,  $\text{C}_{7-10}$  phenylalkyl, lower acyl, or



H

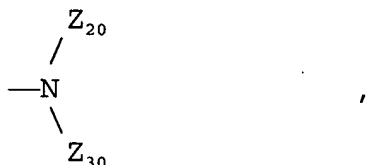
where  $R_{22}$  is any of H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl, or lower acyl; provided that, when one of  $R_5$  or  $R_6$  is  $-NR_{22}$ , the other is H;

(II):



wherein  $Z_1$  is the identifying group of any of the amino acids Gly, Ala, Val, Leu, Ile, Ser, Asp, Asn, Glu,  $\beta$ -Nal, Gln, p-X-Phe (where X = H, F, Cl, Br,  $NO_2$ , OH or  $CH_3$ ),  $F_5$ -Phe, Trp, Cys, Met, Pro, or HyPro; and each  $Z_2$ ,  $Z_3$ , and  $Z_4$ , independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; or

(III):



wherein each  $Z_{20}$  and  $Z_{30}$ , independently, is H, lower alkyl, lower phenylalkyl, lower naphthylalkyl; further provided that, when either of  $Z_{20}$  or  $Z_{30}$  is other than H,  $A^7$  is His,  $A^6$  is Gly,  $A^5$  is Val,  $A^4$  is Ala,  $A^2$  is His, and either of  $R_1$  or  $R_2$  is other than H,  $A^1$  must be other than deleted; further provided that, for the formulas (I) through (III), any asymmetric carbon atom can be R, S or a racemic mixture; and further provided that each  $R_1$  and  $R_2$ , independently, is H,  $C_{1-12}$  alkyl,  $C_{7-10}$  phenylalkyl,  $COE_1$  (where  $E_1$  is  $C_{1-20}$  alkyl,  $C_{3-20}$  alkenyl,  $C_{3-20}$  alkynyl, phenyl, naphthyl, or

C<sub>7-10</sub> phenylalkyl), or lower acyl, and R<sub>1</sub> and R<sub>2</sub> are bonded to the N-terminal amino acid of said peptide, and further provided that when one of R<sub>1</sub> or R<sub>2</sub> is COE<sub>1</sub>, the other must be H, or a pharmaceutically acceptable salt thereof.

82 (new): The method of claim 81 wherein said therapeutic peptide is of the formula:

A<sup>0</sup> = Gly, D-Phe, or is deleted;

A<sup>1</sup> = p-Glu, D-Phe, D-Ala, D-β-Nal, D-Cpa, or D-Asn;

A<sup>2</sup> = Gln, His, 1-methyl-His, or 3-methyl-His;

A<sup>4</sup> = Ala;

A<sup>5</sup> = Val;

A<sup>6</sup> = Sar, Gly, D-Phe, or D-Ala;

A<sup>7</sup> = His;

and, where W is (I) and R<sub>3</sub> is CH<sub>2</sub> or CH<sub>2</sub>-CH<sub>2</sub>, Z<sub>1</sub> is the identifying group of Leu or Phe, where W is (I) and R<sub>3</sub> is CHOH-CH<sub>2</sub>, Z<sub>1</sub> is the identifying group of Leu, cyclohexyl-Ala,

or Phe and each R<sub>5</sub> and R<sub>6</sub> is H; and where W is (I), V is NHR<sub>6</sub>, and R<sub>6</sub> is NH<sub>2</sub>; where W is (II), Z<sub>1</sub> is the identifying group of any one of the amino acids Leu or p-X-Phe (where X = H, F, Cl, Br, NO<sub>2</sub>, OH or CH<sub>3</sub>); and each Z<sub>2</sub>, Z<sub>3</sub> and Z<sub>4</sub>, independently, is H, lower alkyl, lower phenylalkyl, or lower naphthylalkyl; and where W is (III), each Z<sub>20</sub> and Z<sub>30</sub>, is H; and each R<sub>1</sub> and R<sub>2</sub>, independently, is H, lower alkyl, or lower acyl.

83 (new): The method of claim 82 wherein said therapeutic peptide is of the formula:

D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-ethylamide.

84 (new): The method of claim 82 wherein said therapeutic peptide is of the formula:

p-Glu-Gln-Trp-Ala-Val-Gly-His-statine-amide.

85 (new): The method of claim 82 wherein said therapeutic peptide is of the formula:

D-Cpa-Gln-Trp-Ala-Val-Gly-His- $\beta$ -Leu-NH<sub>2</sub>.

86 (new): The method of claim 81 wherein said therapeutic peptide is of the formula: W is (I), V is OR<sub>4</sub>, and R<sub>4</sub> is any of C<sub>1-20</sub>alkyl, C<sub>3-20</sub>alkenyl, C<sub>3-20</sub>alkinyl, phenyl, naphthyl, or C<sub>7-10</sub> phenylalkyl, and A<sup>6</sup> is N-methyl-D-Ala or A<sup>1</sup> is D-F<sub>5</sub>-Phe.

87 (new): The therapeutic peptide of claim 86 of the formula:

D-Phe-Gln-Trp-Ala-Val-N-methyl-D-Ala-His-Leu-methylester.

88 (new): The therapeutic peptide of claim 82 of the formula:

D-Cpa-Gln-Trp-Ala-Val-D-Ala-His- $\beta$ -Leu-NH<sub>2</sub>.

89 (new): The method of claim 81 wherein said effective amount is 0.5  $\mu$ g/kg/day to 5 mg/kg/day.